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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/639,076	08/11/2003	Mark S. Dennis	P1639R1C1	6938

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MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER	
ROBINSON, HOPE A	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 07/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/639,076	DENNIS, MARK S.	
	Examiner	Art Unit	
	Hope A. Robinson	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26 and 28-45* is/are pending in the application.

4a) Of the above claim(s) *19-26 and 35-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18,28-34 and 43-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. Applicant's response to the Office Action mailed August 29, 2005 on May 5, 2006, is acknowledged.

Claim Disposition

2. Claims 44-45 have been added. Claims 1-26 and 28-45 are pending. Claims 1-18, 28-34 and 43-45 are under examination.

3. The instant application is now in compliance with the sequence rules.

Withdrawn-Claim Rejections - 35 USC ∋ 101

4. Previous rejections to claims under 35 U.S.C. 101 is withdrawn by virtue of submission of an amendment.

Withdrawn-Claim Rejections - 35 USC ∋ 102

5. Previous rejections to claims under 35 U.S.C. 102 is withdrawn by virtue of submission of an amendment.

New-Claim Objection

6. Claim 1 is objected to because of the following informalities:

Claim 1 is objected to because the following appears that "Trp3 is Trp, Phe, or Tyr,;"

Correction of the above is required.

Maintained and Amended-Claim Rejections - 35 USC ∋ 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-18, 28-34 and 43-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to a peptide comprising the sequence set forth in SEQ ID NO:4, which can be varied with zero to eight substitutions (see for example claim 1). The variables contained in claims encompass any amino acids, for example, replacement of Glu_1, Thr_1, Glu_2, Thr_2 and Glu_3, which encompasses the 20 naturally occurring amino acids and all the uncommon amino acids. In addition, claims 44-45 are directed to a portion of the N or C terminus of a hybrid molecule and no indication is given as to what this structure looks like. In view of the variability encompassed by the claims the claimed peptide might not bind FVII/FVIIa as desired, furthermore, the instant specification does not adequately describe the variability encompassed in the claims to demonstrate possession. Moreover, the claims recite the open language comprising which indicates that

fragments can be added to the N or C terminus of the peptide. A skilled artisan cannot envision the detailed chemical structure of the claimed peptide. Thus the claims lack adequate written description to demonstrate to a skilled artisan that applicant was in possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. See *Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir.1997)*. Therefore, a biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence. For example, even though a genetic code table would correlate a known amino acid sequence with a genus of coding nucleic acids, the same table cannot predict the native, naturally occurring nucleic acid sequence of a naturally occurring mRNA or its corresponding cDNA. *See MPEP 2163.*

Further, *Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir.1991)*, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genus of encoded proteins, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the

complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. *See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993). See MPEP 2163.*

8. Claims 1-18, 28-34 and 43-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the peptide set forth in SEQ ID NO: 4 and the other specific peptides provided in the specification, does not reasonably provide enablement for any portion thereof or the large genus encompassed in the claims (see claims 1 and 44 for example). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. The enablement requirement refers to the requirement that the specification describe how to make and how to use the invention. There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: Quantity of Experimentation Necessary; Amount of direction or guidance presented; Presence or absence of working examples; Nature of the Invention; State of the prior art and Relative skill of those in the art; Predictability or unpredictability of the art and Breadth of the claims (see *In re Wands, 858 F.2d at 737, 8 USPQ2d at1404 (Fed. Cir. 1988*). The factors most relevant to the instant invention are discussed below.

The amount of experimentation required to practice the claimed invention is undue as the claims encompass a large variable genus of peptides. The claims are directed to a peptide

comprising the sequence set forth in SEQ ID NO:4, which can be varied with zero to eight substitutions (see for example claim 1). The variables contained in the claims encompass any amino acids, for example, replacement of Glu_1, Thr_1, Glu_2, Thr_2 and Glu_3, which encompasses the 20 naturally occurring amino acids and all the uncommon amino acids. In addition, claims 44-45 are directed to a portion of the N or C terminus of a hybrid molecule and no indication is given as to what this structure looks like. In view of the variability encompassed by the claims the claimed peptide might not bind FVII/FVIIa as desired, furthermore, the instant specification does not provide adequate guidance with regard to the variability encompassed in the claims. Therefore, a true correlation between structure and function is missing. In view of the foregoing, undue experimentation would be required to practice the claimed invention commensurate in scope with the claims.

Predictability of which potential changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (for example, expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, for example, multiple substitutions. In this case, the necessary guidance has not been provided in the specification. Therefore, while it is known in the art that many amino acid substitutions are possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited, as certain positions in the sequence are critical to the protein's

structure/function relationship. It is also known in the art that a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many cases. For example, various sites or regions directly involved in binding activity and in providing the correct three-dimensional spatial orientation of binding and active sites can be affected (see Wells, Biochemistry, vol. 29, pages 8509-8517, 1990). The instant specification provides no guidance/direction as to which regions of the protein would be tolerant of modifications and which would not, and it provides no working examples of any variant sequence that is encompassed by the claims. It is in no way predictable that randomly selected mutations, such as deletions, substitutions, additions, etc., in the disclosed sequences would result in a protein having activity comparable to the one disclosed. As plural substitutions for example are introduced, their interactions with each other and their effects on the structure and function of the protein is unpredictable. The skilled artisan would recognize the high degree of unpredictability that all the fragments/variants encompassed in the claims would retain the recited function.

The state of the prior art provides evidence for the high degree of unpredictability as stated above. Seffernick et al. (J. Bacteriology, vol. 183, pages 2405-2410, 2001) disclose two polypeptides having 98% sequence identity and 99% sequence identity, differing at only 9 out of 475 amino acids (page 2407, right column, middle and page 2408, Fig. 3). The polypeptides of Seffernick et al. are identical along relatively long stretches of their respective sequences (page 2408, Fig. 3), however, these polypeptides exhibit distinct functions. The modifications exemplified in the Seffernick et al. reference is small compared to those contemplated and encompassed by the claimed invention (see page 21 of the specification and claim 3, for example).

The specification lacks adequate guidance/direction to enable a skilled artisan to practice the claimed invention commensurate in scope with the claims. Furthermore, while recombinant and mutagenesis techniques are known in the art, it is not routine in the art to screen large numbers of mutated proteins where the expectation of obtaining similar activity is unpredictable based on the instant disclosure. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in certain activity, which is very complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited, therefore, the general knowledge and skill in the art is not sufficient, thus the specification needs to provide an enabling disclosure.

The working examples provided do not rectify the missing information in the instant specification pertaining to the claimed variant. The nature and properties of this claim is difficult to ascertain from the examples provided as one of skill in the art would have to engage in undue experimentation to construct the variants of the claimed invention and examine the same for function.

The specification does not provide support for the broad scope of the claims, which encompass a large variable genus of peptides. The issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level artisan and the guidance presented in the instant specification and the prior art of record. This make and test position is inconsistent with the decisions of *In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970)* where it is stated that "...scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in

the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)*. Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art, attempting to construct and test variants of the claimed invention would constitute undue experimentation. Making and testing the infinite number of possible variants to find one that functions as described is undue experimentation. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

Response to Arguments

9. The response filed on May 5, 2006 has been considered. Note that the rejection of record under 35 U.S.C. 112, first paragraph written description remains. Note also that a new objection to the claims and rejection under 35 U.S.C. 112, first paragraph, enablement have been implemented for the reasons stated above.

With regard to the written description rejection, applicant states that this rejection is traversed as compliance with the written description requirement does not require an applicant to describe exactly the subject matter claimed. In addition, applicant opines that possession of a

claimed genus does not require description of every member. This argument is not persuasive. Claim 1 encompasses the structure of SEQ ID NO:4 (Trp_1-Glu_1-Val-Leu-Cys_1-Trp_2-Thr_1-Trp_3-Glu_2-Thr_2-Cys_2-Glu_3-Arg) and can be varied by zero to eight amino acid substitutions. In addition, the claim recites the language comprising which is open, thus any structure can be added to the N or C terminus of the peptide in addition, to the variation below. For example, the structure could be: Phe-Pro-Val-Ala-Cys_1-Tyr-Lys-Phe-Pro-Thr_2-Cys_2-Glu_3-Arg or Met-Ser-Ala-Val-Cys_1-Phe-Pro-Tyr-Glx-Thr_2-Cys_2-Glu_3-Arg and can additionally have a fragment attached to the N or C terminus of any length. Note that this structure is no longer SEQ ID NO:4 and is not exemplified in the specification as binding FVII/FVIIa in an in vitro assay, however, is encompassed the claimed variation. An enormous amount of peptides are encompassed in the claimed genus just by replacing "Glu_1, Thr_1, Glu_2, Thr_2 and Glu_3" with any amino acids that naturally occur or are uncommon, without including the other variability encompassed in the claims such as Trp_1 or adding to the N or C terminus. In addition, there is no indication of a conserved region and the only residues not substituted are the cysteines at position 5 and 11 which by themselves cannot carry the function desired. Applicant at the time of filing the instant application did not demonstrate possession of the genus claimed. Thus, the rejection remains.

Conclusion

10. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr, can be reached at (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hope Robinson, MS

Patent Examiner 4/24/06

HOPE ROBINSON
PATENT EXAMINER